ACUTE TOXICITY SUMMARY

METALLIC COPPER AND COPPER COMPOUNDS

Molecular formula	Molecular weight	Synonyms	CAS Registry Number
Cu	63.55	copper	7440-50-8
CuO	79.54	cupric oxide, copper oxide, copper (I) oxide	1317-38-0
$CuSO_4$	159.60	copper sulfate, blue vitrol, copper (II) sulfate, cupric sulfate, blue copper, blue stone	7758-98-7

I. Acute Toxicity Summary (for a 1-hour exposure)

Inhalation reference exposure level	**100 μg/m³**
Critical effect(s)	respiratory system defense mechanism
Hazard Index target(s)	Respiratory System

II. Physical and Chemical Properties (for metallic copper except as noted)

(HSDB, 1994)

Description	reddish metal
Density	8.94 g/cm^3 @ 25°C
Boiling point	2595°C
Melting point	1083°C
Vapor pressure	1 mm Hg @ 1628°C
Flashpoint	not applicable
Explosive limits	not applicable
Solubility	soluble in nitric acid; very slightly soluble in hydrochloric acid and ammonium hydroxide
Odor threshold	not applicable
Odor description	odorless
Metabolites	no data found
Conversion factor	not applicable

III. Major Uses or Sources

Copper (Cu) is a widely used structural metal, particularly where high electrical and thermal conductivity are needed (ATSDR, 1990). Copper fumes are generated in copper and brass foundries, in smelters, and in the welding of copper-containing metals. Copper compounds are found in fungicides and other agricultural products, ceramics, and pyrotechnics. Airborne sources of copper include combustion of fuels and other materials containing copper.

Copper sulfate ($CuSO_4$), the most common copper salt, is used as a fungicide, as a component of electroplating solutions, as a chemical intermediate for other copper salts in dyes, and in the tanning of leather (ATSDR, 1990).

Copper oxide (CuO) is another common copper salt. It is used in insecticides, fungicides, and catalysts (HSDB, 1994). CuO is also used in fuel additives, cement, and wood preservatives.

IV. Acute Toxicity to Humans

Following occupational exposures to copper dust, commonly reported reactions include metallic or sweet taste, upper respiratory tract irritation, and nausea (Whitman, 1962). An unpublished letter regarding occupational exposure to copper fumes reported that levels of 0.02-0.40 mg/m^3 copper did not "cause complaints" while exposure to 1.0-3.0 mg/m^3 copper for "short periods of time" resulted in a "sweet taste in the mouth" but no nausea (Whitman, 1957).

Inhalation exposure to copper fumes, usually from welding or smelting operations, may result in "metal fume fever." This condition results in headache, dryness of the mouth and throat, chills, fever, and muscle aches, usually beginning 4-8 hours after exposure to the oxides of various metals, including copper. Symptoms and signs spontaneously subside within 24-36 hours (ATSDR, 1990; Seaton and Morgan, 1984). Symptoms consistent with metal fume fever were reported by workers in a facility with airborne copper dust at concentrations of 0.03-0.12 mg/m^3 (Gleason, 1968). Upper respiratory irritation has been reported, in addition to symptoms consistent with metal fume fever (fever, dyspnea, chills, headache, nausea, myalgia, cough, shortness of breath, a sweet metallic taste, and vomiting), in factory workers exposed to copper fumes for 1 to 10 hours as a result of cutting pipes known to contain copper (Armstrong *et al*., 1983). The sweet taste experienced by workers from the Whitman (1957) report above is consistent with the onset of symptoms of metal fume fever.

Factory workers exposed to copper dust, CuO, and several other copper salts reported symptoms of eye, nose, and throat irritation, anorexia, and nausea (Askergren and Mellgren, 1975; Suciu *et al*., 1981). Occasional diarrhea was also reported by these workers.

Predisposing Conditions for Copper and Copper Compound Toxicity

Medical: Persons with Wilson's disease, a genetic disorder affecting copper homeostasis, may be more sensitive to the effects of copper exposure (Schroeder *et al*., 1966; ATSDR, 1990). Persons with glucose-6-phosphate dehydrogenase deficiency, anemic, allergic, liver or kidney conditions moght be more sensitive (Reprotext, 1999). Infants and children less than 1-year of age may be more sensitive to the effects of copper exposure because homeostatic mechanisms for clearing copper from the body are not yet developed

Chemical: Persons exposed to molybdenum might be less sensitive to copper, since molybdewnum is antagonistic to copper toxicity (Reprotext, 1999).

V. Acute Toxicity to Laboratory Animals

Rats were dosed by intratracheal instillation with 2.5, 5, 10, 20, 30, 50, and 100 mg Cu/rat and pulmonary clearance of CuO was measured over time (Hirano *et al*., 1993). The CuO particles were cleared from the lung with a half-time of 37 hours.

A 54% and 70% increase in mortality in male and female mice, respectively, over controls was observed following challenge with aerosolized streptococci after a 3-hour exposure to 0.56 mg/m³ Cu as $CuSO_4$ (Drummond *et al*., 1986). Pulmonary bactericidal activity was not measured for this exposure group.

The effects of copper sulfate (and other metal sulfate) aerosols on respiratory defense mechanisms were studied in male hamsters (Skornik and Brain, 1983). Pulmonary macrophage phagocytic rates were measured by determining the in vivo uptake of radioactive colloidal gold 1, 24, or 48 hours after a single 4-hour inhalation exposure to 0, 0.3, 3.2, 4.0, 5.8 and 7.1 mg Cu/m³. When hamsters were exposed for 4 h to greater than or equal to 3.2 mg Cu/m³, macrophage endocytosis was significantly reduced 1 h after exposure compared with that in unexposed control animals. The reduction was dose-dependent. At 24 h after exposures to the higher concentrations of Cu the percent of gold ingested by pulmonary macrophages remained depressed but less than at 1 hour. (By 48 h, the rate of macrophage endocytosis in hamsters returned to control levels except in hamsters exposed to 3.2 and 5.8 mg Cu/m³.)

VI. Reproductive or Developmental Toxicity

Copper is known to be spermicidal (U.S.EPA, 1987). Copper absorbed from copper intrauterine loops or wires has been shown to prevent mammalian embryogenesis. Conversely, terata have been observed in the offspring of experimental animals deficient in dietary copper.

Inhibited spermatogenesis and testicular atrophy were observed in male rats exposed to 0.1-1.0 mg/m³ CuO (Ginoian, 1976). The same study also reported that the number of fetuses was reduced in a dose-related manner in females exposed to CuO. Because the original article was not available for review, key experimental details, including duration of exposure, are unknown.

VII. Derivation of Acute Reference Exposure Level and Other Severity Levels (for a 1-hour exposure)

Reference Exposure Level (protective against mild adverse effects): 100 μg/m³

Study	ACGIH, 1991; Gleason, 1968; Whitman, 1957, 1962
Study population	workers
Exposure method	inhalation
Critical effects	metal fume fever
LOAEL	unkown
NOAEL	1 mg Cu/m³

Exposure duration	unknown
Extrapolated 1 hour concentration	no extrapolation
LOAEL uncertainty factor	1
Interspecies uncertainty factor	1
Intraspecies uncertainty factor	10
Cumulative uncertainty factor	10
Reference Exposure Level	0.1 mg Cu/m³ (100 µg/m³)

The ACGIH-TLV is based on an unpublished letter which reported that exposure to 1 - 3 mg/m^3 copper fume for "short periods" resulted in a "sweet taste in the mouth" and that exposure to 0.02 - 0.4 mg/m^3 did not result in any symptoms (Whitman, 1957). However, it was not clear from the letter if or how actual copper levels were measured. Another author reported that symptoms of metal fume fever were observed in workers exposed for an unspecified number of weeks to 0.03 - 0.12 mg/m^3 copper dust (Gleason, 1968). The latter exposure was not designed to determine the level of copper responsible for the symptoms; it was meant to justify the implementation of exhaust controls. Therefore, the air samples were not directly compared to worker exposure or worker symptoms.

The current REL is based on the ACGIH-TLV of 1 mg/m^3 copper dust. The TLV of 1 mg/m^3 is a NOAEL based on the report of Whitman (1957) indicating that exposure to copper dust was detectable by taste but that no other symptoms occurred following exposure to 1 - 3 mg/m^3 for an unknown duration. An uncertainty factor of 10 was applied to the NOAEL to account for variability in individual response. No time extrapolation was applied because the duration of exposure was not clearly specified by either of the available reports. Because of the limitations of the existing data, reevaluation of the REL for copper is recommended when better methods or data are available.

Level Protective Against Severe Adverse Effects

No recommendation is made due to the limitations of the database.

Level Protective Against Life-threatening Effects

No recommendation is made due to the limitations of the database.

NIOSH (1995) lists an IDLH of 100 mg/m³ but it is based on studies of lethality by the oral route in animals and man.

VIII. References

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Whitman NE. Letter to TLV Committee from Industrial Health Engineering. Bethlehem (PA): Bethlehem Steel Co; 1962 (April 24, 1962).